

**UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS**

ASTELLAS INSTITUTE FOR REGENERATIVE
MEDICINE, and STEM CELL & REGENERATIVE
MEDICINE INTERNATIONAL, INC.,

Plaintiffs,

v.

IMSTEM BIOTECHNOLOGY, INC., XIAOFANG
WANG, and REN-HE XU,

Defendants.

C.A. No. 1:17-cv-12239

**LEAVE TO FILE GRANTED
ON 10/3/19 (DKT. 111)**

DEFENDANTS' SECOND AMENDED ANSWER

Defendants ImStem Biotechnology, Inc. (“ImStem”) Dr. Xiaofang Wang, M.D., Ph.D. (“Dr. Wang”) and Dr. Ren-He Xu (“Dr. Xu”) (collectively “Defendants”) hereby answer the First Amended Complaint of plaintiffs Astellas Institute for Regenerative Medicine (“Astellas”) and Stem Cell & Regenerative Medicine International, Inc. (“SCRMI”) (collectively “plaintiffs”) as follows:¹

INTRODUCTION

1. Defendants admit that this action concerns the creation of mesenchymal-stem-like-cells (“mesenchymal stem cells,” “HB-MSCs” or “MSCs”) and that such cells are useful in treating various disorders, including multiple sclerosis. Defendants deny the remaining allegations contained in Paragraph 1.

2. Defendants admit that Astellas and SCRMI focus on research regarding

¹ Per the Court’s order (Dkt. 111 at 6-7), Defendants are not re-filing their Amended Counterclaims, which remain part of the pleadings and can be found at Dkt. 91 at 12-23.

regenerative medicine. Defendants further admit that Dr. Lu and Dr. Lanza published an article in Nature Methods in 2007 on a method for generating hemangioblasts from embryonic stem cells. Defendants admit that hemangioblasts are a specialized type of progenitor cell derived from human embryonic stem cells that are useful in the field of regenerative medicine because they can be differentiated into a number of different cell types used for the treatment of various diseases. Defendants lack knowledge or information sufficient to admit or deny the remaining allegations contained Paragraph 2.

3. Defendants admit that Dr. Kimbrel and Dr. Lanza developed a method for differentiating embryonic stem cells into mesenchymal stem cells via a hemangioblast intermediate. Defendants deny that Dr. Kimbrel and Dr. Lanza thought of the idea of using the mesenchymal stem cells they created to treat autoimmune diseases like multiple sclerosis. Defendants lack knowledge or information sufficient to admit or deny the remaining allegations contained Paragraph 3.

4. Defendants deny that SCRMI was a small company at the time. Upon information and belief, SCRMI was a subsidiary of a publicly traded company. Defendants admit the remaining allegations contained in Paragraph 4.

5. Defendants deny that Dr. Lu knew that defendants had access to the EAE mouse model. Defendants admit that Dr. Lu introduced Dr. Wang to Dr. Kimbrel to discuss a potential collaboration in response to an inquiry from Dr. Wang. Defendants deny that “[t]he parties agreed in writing that in exchange for providing these proprietary cells, data and know how, Defendants would not disclose these materials to third parties.” Defendants admit that Dr. Kimbrel and Drs. Xu and Wang corresponded, but deny that such correspondence comprises or constitutes a written or binding agreement or contract. Defendants admit that plaintiffs

possessed certain technology related to generating mesenchymal stem cells and that they shared such information with Defendants for purposes of the collaboration. Defendants admit that Dr. Xu submitted a grant application in January 2011 for further studies on the use of MSCs in the EAE model. Defendants lack knowledge or information sufficient to admit or deny the remaining allegations contained in Paragraph 5.

6. Defendants admit that the test results from the EAE mouse experiments were positive and that Dr. Kimbrel, Dr. Xu and Dr. Wang worked together on an article that was published in Stem Cell Reports in July 2014. Defendants deny the remaining allegations contained in Paragraph 6.

7. Defendants admit that Dr. Xu and Dr. Wang formed ImStem in or about June 2012 and filed Application No. 14/413,290 with the United States Patent and Trademark Office, which became Patent No. 9,745,551 (the “551 Patent”). Defendants further admit that they represented to the PTO that they had invented a method for differentiating mesenchymal stem cells from hemangioblasts using a GSK3 inhibitor and feeder free culture medium. Defendants deny the remaining allegations contained in Paragraph 7.

8. Denied.

NATURE OF THE ACTION

9. Paragraph 9 contains legal conclusions to which no response is required.

THE PARTIES

10. Defendants lack knowledge or information sufficient to admit or deny the allegations contained in Paragraph 10.

11. Defendants lack knowledge or information sufficient to admit or deny the allegations contained in Paragraph 11.

12. Admitted.

13. Admitted.

14. Defendants admit that Dr. Xu was the Chief Scientific Officer of ImStem as well as one of ImStem's founders and is currently employed by the University of Macau. Defendants deny the remaining allegations contained in Paragraph 14.

SUBJECT MATTER JURISDICTION AND VENUE

15. Paragraph 15 contains legal conclusions to which no response is required.

16. Paragraph 16 contains legal conclusions to which no response is required.

17. Paragraph 17 contains legal conclusions to which no response is required.

PERSONAL JURISDICTION

18. Admitted.

19. Admitted.

20. Defendants admit that Dr. Wang and Dr. Xu visited plaintiffs' facility in Marlborough, Massachusetts during their collaboration with Dr. Kimbrel and Dr. Lanza for various reasons, including to collect cells and other materials necessary for their work in the collaboration. Defendants deny the remaining allegations contained in Paragraph 20.

21. Admitted.

22. Admitted.

23. Admitted. Further answering Paragraph 23, Defendants aver that they had their own grant funding to conduct the MSC studies and often used their own grant funds to purchase materials in furtherance of the collaboration.

24. Defendants admit that they traveled to plaintiffs' Marlborough, Massachusetts facility during their collaboration. Defendants deny the remaining allegations contained in

Paragraph 24.

25. Paragraph 25 contains legal conclusions to which no response is required.

26. Paragraph 26 contains legal conclusions to which no response is required.

27. Paragraph 27 contains legal conclusions to which no response is required.

28. Paragraph 28 contains legal conclusions to which no response is required.

FACTUAL BACKGROUND

Plaintiffs' Development of Methods for Generating Mesenchymal Stem Cells

29. Defendants admit that Dr. Kimbrel and Dr. Lanza developed a method for generating hemangioblasts. Defendants admit that hemangioblasts are a specialized type of progenitor cell derived from human embryonic stem cells that are useful in the field of regenerative medicine because they can be differentiated into a number of different cell types used for the treatment of various diseases. Defendants deny the remaining allegations contained in Paragraph 29.

30. Defendants admit that Dr. Lu and Dr. Lanza, along with others, published an article in Nature Methods in 2007 on a method for generating hemangioblasts from embryonic stem cells. Defendants aver that the article published by the journal Nature Methods speaks for itself and requires no further response.

31. Defendants lack knowledge or information sufficient to admit or deny the allegations contained in Paragraph 31.

32. Defendants deny that Dr. Kimbrel and Dr. Lanza thought of the idea to use the mesenchymal stem cells they created to treat autoimmune diseases like multiple sclerosis. Defendants lack knowledge or information sufficient to admit or deny the remaining allegations contained Paragraph 32.

Plaintiffs' Collaboration with Drs. Xu and Wang

33. Defendants deny that Dr. Kimbrel and Dr. Lanza sought to find collaborators with animal facilities and experience with animal models of autoimmune diseases, including the EAE mouse model. Defendants admit the remaining allegations contained in Paragraph 33.

34. Defendants admit Dr. Lu introduced Dr. Kimbrel to Dr. Wang about a potential collaboration and that Dr. Wang suggested testing the mesenchymal stem cells in the EAE mouse model. Defendants deny that Dr. Lu knew that they had access to the EAE mouse model. Defendants lack knowledge or information sufficient to admit or deny the remaining allegations contained in Paragraph 34.

35. Defendants admit that they visited SCRMI in or about August 2010 and collected frozen MSCs for experiments in furtherance of the parties' collaboration. Defendants further admit that, following the meeting at SCRMI, Dr. Kimbrel shared a protocol for differentiating hemangioblasts into MSCs based largely on the protocol that Dr. Lu and Dr. Lanza had previously published in Nature Methods. Defendants deny the remaining allegations contained in Paragraph 35.

36. Defendants deny that Dr. Kimbrel and Dr. Lanza provided data that demonstrated that the cells generated from their protocol were, in fact, mesenchymal stem cells. Defendants admit the remaining allegations contained in Paragraph 36.

37. Admitted.

38. Defendants lack knowledge or information sufficient to admit or deny the allegations contained in Paragraph 38.

39. Defendants admit that a Material Transfer Agreement was proposed but never executed. Defendants deny that they "agreed to" any "understanding." Defendants deny that

“Dr. Kimbrel memorialized the parties’ contract covering confidential [MSC] information and materials that Astellas had shared with Defendants during the course of the collaboration.”

Defendants aver that the quotes in this Paragraph 39 are excerpts from longer documents that speak for themselves and do not require a response. Defendants deny that such documents constitute or created a binding “contract” or agreement. Defendants deny that such documents set forth “written terms under which the collaboration would continue.” Defendants deny that, individually or collectively, they agreed to “abide by the terms” of the alleged contract or agreement. Defendants deny the remaining allegations contained in Paragraph 39.

40. Defendants admit that in the course of the parties’ collaboration, and in connection with the work performed by defendants during that collaboration, they requested certain supplies from Drs. Kimbrel and Lanza.

41. Admitted.

42. Denied.

43. Defendants admit that they continued collaborating with Dr. Kimbrel and Dr. Lanza during 2012 through 2013, including working together to draft an article that was published in Stem Cell Reports. Defendants further admit that discord developed as a result of Dr. Kimbrel and Dr. Lanza’s decision to publish their own paper separately in a lesser-known journal, causing the collaboration’s paper to be rejected from the journal to which it was submitted for publication Cell Stem Cell. Defendants deny all remaining allegations contained in Paragraph 43.

44. Admitted.

45. Admitted.

Dr. Xu and Dr. Wang Form ImStem and File Patent Application

46. Defendants admit that in or about June 2012, they formed ImStem Biotechnology, Inc. and were awarded funding and lab space for stem cell research. Defendants deny the remaining allegations contained in Paragraph 46.

47. Defendants admit that in or about July 2012 and February 2013, they filed the provisional applications that led to the '551 Patent. The '551 Patent claims a method for differentiating hESCs into MSCs using a GSK3 inhibitor and feeder free culture medium. Dr. Wang's method is materially different from the protocol that Dr. Kimbrel shared with Dr. Wang for purposes of their collaboration. Dr. Wang developed his method through his own efforts, separate and apart from the work of the collaboration. Dr. Wang further never disclosed the GSK3 inhibitor method to Dr. Kimbrel or anyone else. Defendants deny the remaining allegations contained in Paragraph 47.

48. Defendants admit that they knew Dr. Kimbrel and Dr. Lanza had filed a patent application on their protocol for differentiating hemangioblasts into MSCs. Defendants further admit that they signed a declaration dated January 12, 2017, stating that they possessed the subject matter of the '551 Patent before November 30, 2011. Further answering Paragraph 48, defendants state that they believed Dr. Kimbrel and Dr. Lanza's protocol for differentiating MSCs contained only obvious, public information. Defendants therefore did not believe that Dr. Kimbrel and Dr. Lanza had contributed anything significant to Dr. Wang's method of differentiating MSCs using a GSK3 inhibitor and feeder free culture medium.

49. Admitted.

50. Defendants admit that plaintiffs possessed certain technology related to generating mesenchymal stem cells and that they shared such information with defendants for

purposes of the collaboration. Defendants deny that the '551 Patent claims plaintiffs' technology. Dr. Wang developed the method claimed in the '551 through his own efforts, separate and apart from the work of the collaboration. Defendants deny the remaining allegations contained in Paragraph 50.

COUNT I

(Correction of Inventorship for the '551 Patent: Drs. Kimbrel and Lanza as Sole Joint Inventors)

- 51. Defendants' answers to Paragraphs 1-50 are incorporated herein by reference.
- 52. Denied.
- 53. Denied.
- 54. Denied.

COUNT II

(In the Alternative, Correction of Inventorship for the '551 Patent: Drs. Kimbrel and Lanza as Joint Inventors with the Currently Named Inventors)

- 55. Defendants' answers to Paragraphs 1-54 are incorporated herein by reference.
- 56. Denied.
- 57. Defendants lack knowledge or information sufficient to admit or deny the allegations in Paragraph 57.

- 58. Denied.

COUNT III
(Conversion)

- 59. Defendants' answers to Paragraphs 1-58 are incorporated herein by reference.
- 60. Defendants admit that plaintiffs possessed certain technology related to generating mesenchymal stem cells and that they shared such information with defendants for purposes of the collaboration. Defendants deny that plaintiffs initially shared this information under strict restrictions regarding its use. Defendants deny the remaining allegations contained

in Paragraph 60.

61. Denied.

62. Defendants deny that Plaintiffs “first became aware of Defendants intended wrongful use of Plaintiffs’ confidential information around July 2015, when the patent application for Defendants ‘551 patent (No. US 2015/0203820) was published.” Defendants admit that WO14011407, an international patent application, has the substantively identical specification and figures as the ‘551 patent, as well as the application that lead to the ‘551 patent. Defendants admit that Plaintiffs became aware of WO14011407 shortly after it was published (on January 16, 2014), but are without knowledge or information regarding the precise date identified in Paragraph 62 (February 4, 2014). Defendants deny that all of Plaintiffs claims “did not arise until after the ‘551 patent issued on August 29, 2017.” Plaintiffs’ allegations as to when they had a right of action on inventorship is a legal conclusion to which no response is required. Defendants deny the remaining allegations contained in Paragraph 62.

63. Denied.

COUNT IV
(Unjust Enrichment)

64. Defendants’ answers to Paragraphs 1-63 are incorporated herein by reference.

65. Denied.

66. Denied.

67. Denied.

68. Denied.

69. Denied.

70. Denied.

COUNT V
(Unfair Trade Practices Under Massachusetts General Law Chapter 93A)

- 71. Defendants' answers to Paragraphs 1-70 are incorporated herein by reference.
- 72. Paragraph 72 contains legal conclusions to which no response is required.
- 73. Denied.
- 74. Denied.
- 75. Denied.
- 76. Denied.

COUNT VI
(Misappropriation of Trade Secrets)

- 77. Defendants' answers to Paragraphs 1-76 are incorporated herein by reference.
- 78. Defendants admit that they received certain scientific information relating to the generation of MSCs during the course of the parties' collaboration. Defendants deny the remaining allegations contained in Paragraph 78.

79. Defendants admit that sometime after the parties' collaboration had commenced Dr. Kimbrel sought assurances that any new information shared by plaintiffs going forward would be treated confidentially for the purposes of further collaboration between the parties. Defendants deny the remaining allegations contained in Paragraph 79.

- 80. Denied.
- 81. Denied.

COUNT VII
(Negligent Misrepresentation)

- 82. Defendants' answers to Paragraphs 1-81 are incorporated herein by reference.
- 83. Defendants admit that sometime after the parties' collaboration had commenced Dr. Kimbrel sought assurances that any new information shared by plaintiffs going forward

would be treated confidentially for the purposes of further collaboration between the parties. Defendants further admit that on or about January 12, 2017 they filed a declaration with the United States Patent and Trademark Office declaring that they are the original inventors of the subject matter of the '551 Patent. Defendants deny the remaining allegations contained in Paragraph 83.

84. Denied.

**COUNT VIII
(Breach of Contract)**

85. Defendants' answers to Paragraphs 1-84 are incorporated herein by reference.

86. Denied.

87. Denied.

88. Defendants admit that Plaintiffs possessed certain technology related to generating a specific type of mesenchymal-stem-like-cells (although not yet confirmed or characterized at the time of their first meeting) and that they shared such information with Defendants for purposes of the joint collaboration, but deny the remaining allegations contained in Paragraph 88.

89. Denied.

90. Denied.

JURY DEMAND

91. Paragraph 91 does not require a response.

PRAYER FOR RELIEF

92. Defendants deny that plaintiffs are entitled to the relief requested in the Complaint. To the extent that any statement in the Prayer for Relief is deemed factual, it is denied.

AFFIRMATIVE DEFENSES

Further answering the First Amended Complaint, Defendants assert the following defenses, without assuming the burden of proof where such burden would otherwise be on Plaintiffs. Defendants reserve the right to assert additional defenses as further information is obtained.

FIRST AFFIRMATIVE DEFENSE (Failure to State a Claim)

The First Amended Complaint fails to state a claim upon which relief may be granted.

SECOND AFFIRMATIVE DEFENSE (Laches)

Plaintiffs' claims are barred, in whole or in part, by the doctrine of laches.

THIRD AFFIRMATIVE DEFENSE (Unclean Hands)

Plaintiffs' claims are barred, in whole or in part, by the doctrine of unclean hands.

FOURTH AFFIRMATIVE DEFENSE (Statute of Limitations)

Plaintiffs' claims are barred, in whole or in part, by the applicable statute of limitations.

FIFTH AFFIRMATIVE DEFENSE (Failure of Consideration)

Claim VIII is barred, in whole or in part, by a failure of consideration.

SIXTH AFFIRMATIVE DEFENSE (Statute of Frauds)

Claim VIII is barred, in whole or in part, by the statute of frauds.

SEVENTH AFFIRMATIVE DEFENSE (Lack Meeting of the Minds)

Claim VIII is barred, in whole or in part, by a lack of meeting of the minds.

**EIGHTH AFFIRMATIVE DEFENSE
(No Damages)**

Claim VIII is barred, in whole or in part, because Plaintiffs were not damaged in the manner alleged, or at all, by any act or admission of Defendants.

**NINTH AFFIRMATIVE DEFENSE
(Failure to Mitigate)**

Claim VIII is barred, in whole or in part, by Plaintiffs' failure to mitigate their alleged damages, if any.

October 17, 2019

Respectfully submitted,

DEFENDANTS IMSTEM
BIOTECHNOLOGY, INC., DR.
XIAOFANG WANG, and DR. REN-HE XU

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CERTIFICATE OF SERVICE

I hereby certify that on October 17, 2019, I caused a true copy of the foregoing document to be served upon all counsel of record via the Court's CM/ECF electronic filing system.

/s/ Benjamin M. Stern

Benjamin M. Stern